REMARKS/ARGUMENTS

Re-examination and favorable reconsideration in light of the above amendments and the following comments are respectfully requested.

Claims 1 - 35 are pending in the application. Currently, claims 1 - 4, 10 - 18, and 26 - 35 stand rejected and claims 5 - 9 and 19 - 25 stand withdrawn from consideration as being directed to a non-elected invention.

By the present amendment, claims 3 has been amended and claim 29 has been cancelled.

In the office action mailed September 2, 2003, claims 1 - 4, 10 - 18, and 26 - 35 were rejected under 35 U.S.C. 112, first paragraph as being non-enabling; claims 1 - 4, 10 - 18, and 26 - 35 were rejected under 35 U.S.C. 112, first paragraph, as lacking a written description; claims 3 and 29 were rejected under 35 U.S.C. 112, second paragraph; claims 1 - 4, 14, and 26 - 35 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,455,686; and claims 1 - 4, 10 - 13, 15 - 18, 34, and 35 were rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,455,686 in view of U.S. Patent No. 4,302,458 and U.S. Patent No. 6,258,816 or U.S. Patent No. 5,827,852 or U.S. Patent No. 6,319,513.

The foregoing rejections are traversed by the instant response.

The present invention relates to pharmaceutical compositions for the prevention and treatment of allergies. The present invention offers a new means of treating allergies that are both preventive and curative. For example, as pointed out on page 12, lines 8 - 9 of the specification, the compositions of the present invention may be given as a preventive measure to children of allergic parents. In fact, one of the advantages to the compositions of the present invention is that the compositions can be given to anyone and everyone.

In accordance with the present invention, an anti-allergic pharmaceutical composition contains at least active agents chosen from among: (i) one allergen; (ii) one antihistamine compound, and (iii) one inhibitor of histamine synthesis. The active agents in the composition are associated in the composition with a pharmaceutically acceptable vehicle. The allergen may be chosen from among the major antigens or may be a mixture of major antigens of acarids able to induce an immune reaction. The antihistamine compound is preferably chosen from the group comprising: brompheniramine, cetirizine, fexofenadine, cyproheptadine, dexchlorpheniramine, hydroxizine, ketotifene, loratidine, mequitazine, oxotomide, mizolastine, ebastine, astemizole, carbinoxamide, alimemazine, buclizine, cyclizine hydrochlorate, and doxylamine.

With respect to the rejection under 35 U.S.C. 112, first paragraph, for lack of enablement, the Examiner has taken the position that the instant specification is only enabling for (1) an anti-allergic pharmaceutical composition comprising at least two active agents selected from the group consisting of (i) dust mite allergen peptides selected from the group consisting of SEQ ID NO: 3 - 5, (ii) one antihistamine compound such as the ones recited in claim 10, (iii) one inhibitor of histamine synthesis wherein the inhibitor of histamine synthesis is tritoqualine which is also an inhibitor of histidine decarboxylase for treating allergic hypersensitivity by reduction of allergic reaction both on the upstream phase of IgE synthesis and reduction on the downstream phase of histamine synthesis and release; (2) the anti-allergic pharmaceutical composition comprising (i) at least one allergen peptides selected from D Pteronyssinus and D. Farinae, and (ii) at least one anthistamine compound such as the one recited in claim 10, and a pharmaceutically acceptable vehicle; (3) the pharmaceutical composition wherein the allergen is a major allergen of acarids or a mixture of allergen selected from the group consisting of SEQ UD NO. 3 - 4; (4) the pharmaceutical composition wherein the allergen is of the order of 1 to 1500 μg or from 10 to 150 μg; (5) the pharmaceutical composition wherein the antihistamine compound is of the order of 1 to 2000 mg or from 5 to 200 mg.;

and (7) the pharmaceutical composition further comprising an inhibitor of histamine synthesis wherein the inhibitor of histamine synthesis is an inhibitor of histidine decarboxylase tritoqualine between 10 and 300 mg and wherein the antihistamine compound is from 5 to 200 mg for treating allergic hypersensitivity by reduction of allergic reaction on both the upstream phase of IgE; and synthesis and reduction on the downstream phase of histamine synthesis and release in children, adults, and infants. The Examiner contends that the specification does not reasonably provide enablement for (1) any anti-allergic pharmaceutical composition as set forth in claims 1 - 3 or (2) any pharmaceutical composition as set forth in claims 4, 10 - 18, and 26 - 32 for preventing any allergic hypersensitive reaction.

It is submitted that the Examiner has not set out a proper case of non-enablement. As set forth in *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993), the Patent Office has the burden of setting forth a reasonable explanation as to why it believes that the scope of protection presented by the claim is not adequately enabled by the disclosure of the invention provided in the specification. This includes providing sufficient reasons for disproving any assertions in the specification as to the scope of enablement. The Examiner has failed to meet this burden. No reasons have been provided by the Examiner as to why

the disclosure in the instant specification does not enable any anti-allergic pharmaceutical composition or any pharmaceutical composition for preventing any allergic hypersensitive reaction. This is precisely what the specification has enabled. Applicants have described exactly how to obtain the claimed compositions in a manner commensurate with the scope of the claims.

The Examiner avers that the disclosure requires undue amount of experimentation but offers no reasons why this is necessary. Applicants have disclosed exactly what is needed to make and use the claimed compositions given the fact that the level of skill in this art is quite extraordinarily high. What level of experiment is undue must be made from the viewpoint of persons experienced in the field of invention. *Elan Pharmaceutical Inc. v. Mayo Foundation for Medical Education and Research*, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003). A considerable amount of experimentation is permissible if the specification provides a reasonable amount of guidance with respect to direction in which the experiments should proceed. See *In re Jackson*, 217 USPQ 804, 817 (Bd. Pat. App. 1982). Given the road map provided by Applicants in the instant specification, there is no question that one of skill in this art could produce compositions commensurate with the claims given the teachings in the instant specification. The Examiner offers no reason why this is not the case given the disclosure in the instant

application. The fact that the specification discloses only two allergens is not dispositive on the issue of undue experimentation being required. Someone who is looking to prevent or treat any allergy could provide an effective pharmaceutical composition using the teachings contained in the instant application.

As to the issue of "preventing", the specification does provide guidance as to how select or identify an individual before allergy symptoms begin, e.g. children who parents have allergies. Further, as set out on page 12, lines 8 - 9 of the specification, anyone can be given the pharmaceutical composition as a preventive measure. Standard tests exist to identify those more susceptible to allergies. Applicants need not disclose such tests because one skilled in the art would be familiar with them. Applicants' invention is related to pharmaceutical compositions, not tests for identifying those who would suffer from allergies.

For these reasons, the Examiner is hereby requested to withdraw the rejection on grounds of non-enablement.

With regard to the rejection under 35 U.S.C. 112, first paragraph, on written description grounds, the Examiner has not sustained his burden of pointing out why the written description does not show that Applicants possessed the claimed invention. The specification in the instant application conveys with

reasonable clarity to those skilled in the art that Applicants, as of the filing date of the application, were in possession of the claimed invention. It should also be noted that the language in the written description in the instant application is commensurate with the language of the claims. To say that Applicants were not in possession of the claimed invention is incorrect. For these reasons, this grounds of rejection should be withdrawn.

With regard to the rejection under 35 U.S.C. 112, second paragraph, claim 29 has been cancelled and claim 3 has been amended to overcome the objections raised by the Examiner. Thus, the rejection is now moot.

Claims 1 - 4, 14, and 26 - 33 are allowable over the '686 patent to McCall et al. It is again submitted that the McCall et al. patent does not teach or suggest the subject matter of the aforementioned claims. The McCall et al. patent relates to the identification of proteins, especially of D. Farinae, and their use in diagnostic or therapeutic techniques to identify or desensitize a subject susceptible to an allergic response to mite. The composition disclosed in this patent might be used in conjunction with other compounds able to modify the function of a cell implied in the hypersensible response. These compounds may be anti-histaminics or compounds which lead the immunoglobulin heavy chain class to switch from IgE to IgG.

These latter compounds are not inhibitors of the synthesis of histamine. The action of these compounds occurs at the end of the allergy reaction, and not upstream. The IgE link is an antigene situated in the basophile. This link provokes liberation of histamine by degranulation of the histamine grains. This involves a biochemical reaction which has nothing to do with the inhibition of the synthesis of histamine. The McCall et al. patent does not disclose the combination of compounds set out in claim 1 and the subject matter set forth in claims 2 - 4, 14, and 26 - 32.

Claims 1 - 4, 10 - 13, 15 - 18, 34 and 35 were rejected under 35 U.S.C. 103(a) as being unpatentable over the '686 patent in view of U.S. Patent No. 4,302,458, and U.S. Patent No. 6,258,816 or U.S. Patent No. 5,827,852, or U.S. Patent No. 6,319,513. It is submitted that the proposed combination of references, assuming one of ordinary skill in the art would combine them in the manner suggested by the Examiner, does not teach or suggest the claimed invention. In particular, none of the patents teach or suggest the combination of compounds set forth in claim 1. The aforementioned comments about the '686 patent are repeated herein by reference. The '458 patent relates to the use of phtalidyl-isoquinolines derivatives, of Noscapine type, to treat allergic conditions. The activity of these compounds is comparable to a tritoqualine inhibitor. The '458

patent would not suggest to one of ordinary skill in the art how to form the compositions of the present invention.

The '816 patent relates to an anti-allergic composition comprising cetrizine. Cetrizine is a histamine antagonist. Nimesulide stabilizes the mast cells, which would prevent the histamine secretion. In a normal situation, histamine can be found in all tissues, and especially in mastocytes. Histamine is stocked in vesicles called granules in basophiles. By stabilizing the mast cells, it is meant to avoid the fusion of the histamine vesicles with the membrane and the consequent liberation of the histamine stock. This action is really downstream compared to the action of an inhibitor of the synthesis of histamine. It is not understood by Applicants how this patent in combination with the others would lead one of ordinary skill in the art to the claimed invention.

The '852 patent relates to a pharmaceutical composition containing anti-histaminic compounds for treating allergies. Here again, it is not understood how this patent would lead one of ordinary skill in the art to the compositions of the claimed invention.

The '513 patent also discloses a pharmaceutical composition containing anti-histaminic compounds for treating allergies. Here again, it is not understood how this patent would lead one

of ordinary skill in the art to the compositions of the claimed invention.

At best, the Examiner has found individual materials used in the compositions of the present invention. Using the blueprint provided by Applicants, the Examiner then attempts to piece the prior art patents together to arrive at the claimed invention. This is nothing more than a classic hindsight rejection. It is submitted that none of these references recognizes the invention made by Applicants and most certainly would not lead one of ordinary skill in the art to make and use the claimed compositions.

None of the cited and applied references would teach or suggest the composition of claim 1. None of the cited and applied references describes the fact of simultaneously inhibiting the synthesis of histamine and competing histamine fixation. None of the cited and applied references describes or suggests acting at the different levels of the allergic reaction chain as described in the instant application. It should be understood that inhibiting the liberation of histamine is really different from inhibiting the synthesis of histamine and that this is a key point that distinguishes the instant invention from the cited and applied prior art. Without these teachings in the prior art, one would not be motivated to combine the references in the manner suggested by the Examiner on page 16 of

the office action. The references simply do not teach or suggest using a peptide substance such as an acarid allergen in combination with an antihistamine and histamine synthesis inhibitor. This combination produces a synergistic result in that it is able to inhibit the response to all allergens triggering an allergic response both in the proven allergic patient and in a preventive manner. The treatment enabled by the compositions of the present invention is a unique pharmacological treatment which is nonspecific (as far as the allergen is concerned) and treats allergies to pollen, to animal hair and to foodstuffs equally well. This efficacy is based on a novel and unobvious theory if the mechanism of action of allergens on the immune reaction, and also on the role of histamine in the stimulation of TH2 cytokines which is blocked by tritoqauline and antihistamines.

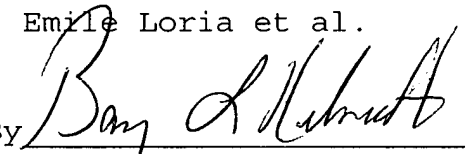
For the foregoing reasons, the instant application is believed to be in condition for allowance.

A notice of appeal is enclosed herewith in the event that the Examiner maintains the rejections of record. Also enclosed is a three (3) month extension of time request and a check in the amount of $1,280.00 to cover the notice of appeal fee and the extension of time fee. Should the Commissioner determine that an additional fee is due, he is hereby authorized to charge said fee to Deposit Account No. 02-0184.

Should the Examiner believe an additional amendment is needed to place the case in condition for allowance, he is hereby invited to contact Applicants' attorney at the telephone number listed below.

Respectfully submitted,

Emile Loria et al.

By 

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I, Nicole Motzer, hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313" on **March 1, 2004**.